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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,964	MATTERN, CLAUDIA	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 4/14/08 are acknowledged.

2. Claim 14 was cancelled.

3. Claims 1-13 and 15-21 are included in the prosecution.

Continued Examination under 37 CFR 1.114

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/14/08 has been entered.

Response to Arguments

Rejection of claims 1-6, 8, and 13-14 under 35 USC § 103(a)

5. Since claim 14 was cancelled, the rejection of claim 14 is moot.

6. Applicant's arguments, see Page 5, filed 2/13/08, with respect to the rejection of claims 1-6, 8, and 13 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) have been fully considered but are not persuasive.

Applicant states that the cited passage of Illum (Col. 7, lines 14-55) is incomplete because there is no disclosure of any active agent. Applicant states that the only complete system formulated by Illum is that containing albumin. This is not found

persuasive because Illum teaches that "the active agent can be incorporated into the microspheres during their formulation or sorbed into/onto the system after preparation" (Col. 7, lines 47-49). In the compositions for the gelatin microspheres and the chitosan microspheres, 90% of olive oil (100ml out of 110ml total solution) and 90% of soybean oil (100ml out of 110ml total solution) was used respectively (Col. 7, lines 14-41). This percentage falls within the claimed range of 60% to 98% of lipophilic carrier of instant claim 1. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the drug delivery composition (with high lipophilic carrier or oil percentage) for the uptake of sex hormone drugs from the nasal cavity, as taught by Illum.

Applicant argues that Ko teaches the creation of an oil phase with roughly 45% (parts-by-weight) of soybean oil (Page 199) and that neither Illum nor Ko teach the use of such high concentrations of lipophilic agents with the active.

This is not found persuasive because Illum teaches a composition with a high level of lipophilic carrier. Ko is used as a secondary reference that provides the teaching of emulsion formulations of testosterone for nasal delivery.

Since all the claimed elements are found in Illum and Ko, one skilled in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Therefore, the rejection of 11/13/07 is maintained.

Rejection of claim 7 under 35 USC § 103(a)

7. Applicant's arguments, see Page 6, filed 2/13/08, with respect to the rejection of claim 7 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Patel et al. (US 6,248,363) have been fully considered but are not persuasive.

Applicant argues that the examiner has failed to show how Patel remedies the deficiencies of Illum and Ko. With respect to claim 7, Patel provides the teaching of macrogolglycerides (as surfactants in formulations which improve the bioavailability of drugs), which is not expressly taught in the primary reference Illum.

Therefore, the rejection of 11/13/07 is maintained.

Rejection of claims 9-10 and 12 under 35 USC § 103(a)

8. Applicant's arguments, see Page 6, filed 2/13/08, with respect to the rejection of claims 9-10 and 12 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Dondeti (International Journal of Pharmaceutics 1996) have been fully considered but are not persuasive.

Applicant argues that Dondeti teaches solid compositions, not liquids, and that Dondeti does nothing to remedy the deficiencies of Illum and Ko. Since the primary reference, Illum, and does not expressly teach viscosity modifying agents, Dondeti is used as a secondary reference to provide the teaching of viscosity modifying agents in formulations for nasal absorption of drugs. Dondeti teaches that: "drugs are usually administered to the nasal cavity in the form of solutions, suspensions, powders,

microspheres, gels or inserts for local or systemic effect" (Page 119, right hand column). Therefore, one skilled in the art would find the teaching of viscosity modifying agents that are used for drug compositions (including solutions) that are administered in the nasal cavity obvious over the teaching provided by Dondeti. The primary reference, Illum, teaches the limitations of the formulation with a high percentage of a lipophilic carrier for the uptake of sex hormone drugs from the nasal cavity, as taught by Illum.

Therefore, the rejection of 11/13/07 is maintained.

Rejection of claim 11 under 35 USC § 103(a)

9. Applicant's arguments, see Page 7, filed 2/13/08, with respect to the rejection of claim 11 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Glass (US 5,897,894) have been fully considered but are not persuasive.

Applicant argues that the examiner has failed to show how Glass remedies the deficiencies of Illum and Ko and that the high lipophilic concentration is absent. This is not found persuasive because the high lipophilic concentration is present in the teaching provided by Illum. Glass provides the teaching of using silicon dioxide as a viscosity increasing or viscosity regulating agent. Since all the claimed elements are found in Illum, Ko, and Glass, one skilled in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Therefore, the rejection of 11/13/07 is maintained.

10. In addition, a double patenting rejection is also being made in view of copending Application No. 11/560,187.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-6, 8, 13, 15-17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998).

Claims are drawn to a lipophilic formulation for nasal application comprising: a) at least one sexual hormone drug in an amount of from 0.5 to 6.0% by weight; b) at least one lipophilic or partly lipophilic carrier, comprising at least one oil in an amount of between 60% and 98% by weight of the formulation; and c) a compound having surface tension decreasing activity in an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water.

Illum teaches a drug delivery system that enhances the uptake of active drug material from the nasal cavity (Col. 1, lines 16-19). The active drugs that can be used in this drug delivery system include sex hormones (Col. 9, line 31). Absorption enhancing materials such as surface active agents are also taught (Col. 5, lines 47-50). A preferred

material is … lysophosphatidylcholine produced from egg or soy lecithin (Col. 5, lines 38-39). Furthermore, "the drug to be administered to a mucosal surface in the … nose could be administered as a viscous solution" (Col. 5, lines 6-8). The drug delivery system comprises microspheres. An emulsification technique using "purified olive oil" (Col. 6, line 48) and "soybean oil" (Col. 7, line 40) was used in the preparation of these microspheres. The microspheres are "made from materials that are known to swell in contact with water to form a gel-like layer with good bioadhesive properties" (Col. 3, lines 5-7).

Illum does not specifically teach a drug delivery system comprising testosterone.

Ko et al. teach emulsion formulations of testosterone for nasal delivery (Abstract). The formulation materials include vegetable oil and surfactants (Page 198, Materials). The formulations are prepared by emulsification of the oil phase (containing the lipophilic testosterone and soybean oil) with the aqueous phase (further containing a surfactant) (Page 199, Preparation of formulations).

It would have been obvious to a person skilled in the art at the time the invention was made to combine the drug delivery system for nasal delivery teaching of Illum with the emulsion formulation of testosterone teaching of Ko to arrive at a nasal delivery system for testosterone. The motivation for combining these references is provided by Illum, which includes sex hormones as drugs that could be used in a nasal drug delivery system. For example, Illum teaches that progesterone "when given by the nasal route … is absorbed effectively with a bioavailability similar to that for an intravenous injection…" (Col. 2, lines 12-13). Furthermore, since testosterone is a sex hormone that

is lipophilic, the inclusion of oil to prepare an emulsion for enhancing the bioavailability of the testosterone and as a slow or sustained release agent would be obvious to a person skilled in the art.

Regarding instant claims 1 and 8, which disclose the weight percentage of component (c) and the sexual hormone drug, a person skilled in the art would modify the percentages of the formulation based on the required dosage and desired release profile, and the recited percentages are obvious variants unless there is evidence of criticality or unexpected results.

13. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) as applied to claims 1-6, 8, 13, and 14 above, and further in view of Patel et al. (US 6,248,363).

The teachings of Illum and Ko are stated above. The difference that Illum and Ko do not teach is the oleoyl macrogolglyceride as the surfactant.

Patel et al. teach that the bioavailability of drugs (like simvastatin) (Col 6, line 49) can be improved by their invention, which includes macrogolglycerides as the surfactant (Col 35, line 46, Col 65, lines 50-53, claim 16). Thus, a person skilled in the art would use a variety of macrogolglycerides for surfactants. These macrogolglycerides would include different fatty acid esters and oleoyl macrogolglyceride since it would be more compatible with humans. The motivation to use these surfactants would be to allow the emulsification and improve the bioavailability of poorly soluble, lipophilic drugs.

14. Claims 9-10, 12 and new claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) as applied to claims 1-6, 8, 13, and 14 above, and further in view of Dondeti (International Journal of Pharmaceutics 1996).

The teachings of Illum and Ko are stated above. The difference not taught by Illum in view of Ko is the viscosity-regulating agent.

Dondeti teaches formulation parameters that affect nasal absorption of drugs. The use of HPMC (hydroxypropyl methylcellulose) (Page 118), methylcellulose (Page 118), and microcrystalline cellulose (Page 125) is taught.

Regarding instant claim 12, a person skilled in the art would modify the percentages of the formulation (specifically percentage of the viscosity regulating agent) in order to optimize the release profile and the recited percentage is an obvious variant unless there is evidence of criticality or unexpected results.

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of Illum and Ko (as stated above), and further use the viscosity modifying agents such as cellulose derivatives taught by Dondeti to arrive at the claimed invention. The motivation to combine these references is provided by Dondeti, who teaches, “increased viscosity prolongs the retention time of drug in the nasal cavity…” (Page 119).

15. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998), and further in view of Glass (US 5,897,894).

The teachings of Illum and Ko are stated above. The difference not taught by Illum in view of Ko is colloidal silicon dioxide as the viscosity-regulating agent.

Glass teaches that "liquid oils can be thickened to increase their viscosity (e.g. with silicon dioxide) (Col. 5, lines 46-48). A person skilled in the art would use colloidal silicon dioxide, which is known in the art as a thickening agent, and would be an obvious choice of materials by the experimenter.

NEW REJECTIONS

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-8, 10-12, 15, 18-19 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-8, 10-12, 16, 18-21 and 24-25 of copending Application No. 11/560,187 ('187 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims and claims of '187 are drawn to a formulation for nasal application comprising at least one hormone drug, at least one lipophilic or partly lipophilic carrier and at least one compound having surface tension decreasing activity, an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water. The difference is that component (b) of instant claim 1 recites the range of the lipophilic carrier as between 60% and 98% by weight of the formulation. It would be obvious to one of ordinary skill in the art to modify the percentage of the lipophilic carrier in the formulation for nasal application during the process of routine optimization. The recited percentage range would have been an obvious variant unless there is evidence of criticality or unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615